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# Double-Frequency Nd:YAG Laser vs. Argon-Green Laser in the Treatment of Proliferative Diabetic Retinopathy: Randomized Study With Long-Term Follow-Up

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***Background and Objective:*** **A randomized clinical trial using the argon-green (514 nm) and the double-frequency Nd:YAG (532 nm) lasers was carried out on 42 eyes with proliferative diabetic retinopathy (PDR), with the aim of assessing the long-term effects of double-frequency Nd:YAG panretinal photocoagulation (PRP).**
***Materials and Methods:*** **Twenty-one eyes were randomized to argon laser treatment (ALT) and 21 to double-frequency Nd:YAG laser treatment (NdLT). The mean follow-up was 28.90 months (± 6.13) in the ALT group and 29.57 months (± 5.17) in the NdLT group.**
***Results:*** **In the ALT group, 20 eyes (95.2%) showed regression of PDR and one eye (4.8%) enlargement of pre-existing new vessels. In the NdLT group, neovascularization regressed in 20 eyes (95.2%) and increased in one (4.8%).**
***Conclusions:*** **The long-term efficacy of double-frequency Nd:YAG laser PRP in the treatment of PDR thus appears to be similar to that of argon-green.** 

**Key words: argon-green laser, double-frequency Nd:YAG laser, panretinal photocoagulation, proliferative diabetic retinopathy**

## INTRODUCTION

The efficacy of argon, krypton, and dye lasers in the treatment of proliferative diabetic retinopathy (PDR) has already been described [1–4]. Unfortunately gas lasers, so far the most widely employed, suffer from several drawbacks, which include high cost, large size, low electrical-to-optical efficiency, large power supply system, and plasma tube degradation with time.

As a possible replacement for these lasers, L'Esperance in 1971 suggested and tested the double-frequency Nd:YAG laser, which combines the advantages of solid state lasers with the emission of monochromatic green wavelength light [5]. However only the technical improvements in frequency doubling technology of these last few years have brought this laser source into clinical practice. The results of the first clinical trial using the double-frequency Nd:YAG laser were published in 1991 [6]. Two groups of ten eyes of patients with proliferative diabetic retinopathy were randomly treated with either the argon-green or double-frequency Nd:YAG lasers. Regression of new vessels and visual outcomes were similar in the two treatment groups after a mean follow-up of 6 months. This report presents a

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TABLE 1. Clinical Characteristics of the 33 Patients in the Two Treatment Groups

| | ALT group | NdLT group |
|---|---|---|
| Age (years) | 44.10 ± 16.22 | 45.00 ± 14.01 |
| Sex (males) | 13 (61.9%) | 11 (52.4%) |
| Diabetes mellitus duration (years) | 15.67 ± 7.65 | 16.19 ± 10.39 |
| Diabetes mellitus type (insulin dependent) | 13 (61.9%) | 14 (66.7%) |
| Initial visual acuity | 0.66 ± 0.22 | 0.69 ± 0.23 |

study with a larger group of treated patients and longer follow-up.

## MATERIALS AND METHODS

Forty-two eyes of thirty-three consecutive patients observed between December 1990 and April 1992 were studied; all had proliferative diabetic retinopathy and fulfilled the inclusion criteria. Each patient provided informed consent for entry to the trial.

Nineteen patients were male and fourteen female and the mean age was 44.45 years ± 14.81. Inclusion criteria were: age at least 18 years, visual acuity of 0.3 or more, PDR with clinically obvious disc new vessels, or neovascularization elsewhere along the vascular arcades (equal to or more than one half the disc area or associated with hemorrhage). Exclusion criteria were: lens opacities and/or vitreous hemorrhages obscuring the fundus, maculopathy reducing visual acuity below 0.3, tractional retinal detachment, and previous laser treatment.

The pretreatment evaluation included a complete examination, determination of best corrected visual acuity (decimal fraction) in each eye, and documentation of retinopathy by fundus photographs and panretinal fluorescein angiography.

The 42 eyes selected for the study were assigned consecutively either to double-frequency Nd:YAG laser treatment (NdLT) or to argon-green laser treatment (ALT). Of the nine patients in whom both eyes were included in the study, the right eye was assigned to NdLT and the left to ALT. The clinical characteristics of the patients in the two treatment groups are shown in Table 1.

ALT was done using a 920 Argon Coherent Medical (Coherent, Palo Alto, CA) and an Argon Ophtalas (Biophysics Medical, Clermont Ferrand, France) and NdLT by a Crystal Focus-Emerald Laser (Biovision, Cournon d'Avergne, France). The treatments were applied through one of three contact lenses: a Goldmann three mirror, a Quadraspheric Volk, or a Mainster Wide-field lens. With the latter two the spot diameter was reduced to obtain retinal spot of a size similar to those produced using the Goldmann lens (500 μm).

The aim of the laser treatment was ablation of non-perfused peripheral and midperipheral retinal areas, avoiding the areas inside the temporal vascular arcades. The mean laser power used in ALT was 484 mW ± 78, and 465 mW ± 63 in NdLT. The two lasers were used in the continuous wave mode and chorioretinal pigmentation of the treated areas influenced the exposure time. The energy parameters, the mean number of spots for each panretinal photocoagulation (PRP), and the mean number of laser sessions needed to complete PRP in the two groups are shown in Table 2.

First control was 6 weeks after treatment. During the first year, visits were scheduled every 3 months and then every 6 months during the second year of follow-up. At each visit a complete examination was made with retinal photographs and fluorescein angiography. Fourteen eyes in the NdLT group and 17 in the ALT group, whose retinal photographs and fluorescein angiograms at the 3 month visit showed no new vessel regression, with persistent areas of retinal non-perfusion. These eyes were retreated. Retreatments were done using the same wavelength each time.

The laser source employed was not known to the ophthalmologist who conducted the follow-up visits and assigned each eye to one of three outcome groups on the basis of analysis of the color photographs and fluorescein angiograms. Eyes showing regression of new vessels were considered improved, while eyes with continued growth of pre existing new vessels or appearance of new ones were considered to have worsened. When there was no change in the size or number of new vessels, eyes were classified as unchanged.

When color photographs appeared to differ from fluorescein angiograms, a second investigator was asked to compare and assess them. All side effects were recorded. Mean follow-up was 28.90 months ± 6.13 in the ALT group and 29.57 months ± 5.17 in the NdLT group. Observed data were analyzed using Fisher's exact test.

**TABLE 2. Parameters Used for Treatment in the Two Groups**

| | ALT group | NdLT group |
|---|---|---|
| Power (mW) | 484 ± 78 | 465 ± 63 |
| Exposure time(s) | CW | CW |
| Spot size (μm) | 500 | 500 |
| Spot number | 1,807 ± 557 | 1,642 ± 337 |
| Session number | 5.27 ± 2.37 | 6.00 ± 2.00 |

**TABLE 3. Evolution of Proliferative Diabetic Retinopathy in the Two Treatment Groups at the end of Follow-Up**

| | ALT group | NdLT group |
|---|---|---|
| Improved | 20 (95.2%) | 20 (95.2%) |
| Unchanged | 0 | 0 |
| Worsened | 1 (4.8%) | 1 (4.8%) |

**TABLE 4. Side Effects in the Two Treatment Groups During and Immediately After Laser Treatment**

| | ALT group | NdLT group |
|---|---|---|
| Vitreous haemorrhage | 2 (9.5%) | 5 (23.8%) |
| Choroidal detachment | 5 (23.8%) | 1 (4.8%) |
| Troublesome pain | 4 (19.0%) | 4 (19.0%) |
| Neurotrophic keratopathy | 3 (14.3%) | 3 (14.3%) |

## RESULTS

In the ALT group one eye was excluded from the study after 28 months of follow-up because of the development of a cataract, which made visualization of the fundus difficult and greatly reduced visual acuity. In the NdLT group one eye had to be excluded after 22 months of follow-up because of central retinal artery occlusion.

The initial mean visual acuity (VA) was 0.66 ± 0.22 in the ALT group and 0.69 ± 0.23 in the NdLT group. The final mean VA in the former was 0.45 ± 0.27 and 0.50 ± 0.25 in the latter. In the ALT group PDR improved in 20 eyes (95.2%) and deteriorated in one (4.8%). In the NdLT group neovascularization regressed in 20 eyes (95.2%) but one eye (4.8%) deteriorated (Table 3). For the two eyes that had to be excluded from the study we assessed visual acuity and the course of PDR on the basis of the findings at the last visit before central retinal artery occlusion and appearance of cataract.

The complications and side effects in the two groups during the follow-up were virtually the same (Table 4). In the NdLT group we observed a larger number of vitreous hemorrhages during and immediately after the laser treatment than in the ALT group (five vs. two), but this difference was not statistically significant. Moreover after 29 months of follow-up, there was no difference in the course of diabetic retinopathy between the two groups. (i.e., the number and size of new vessels and the occurrence of complications, such as vitreous hemorrhage or tractional retinal detachment).

Laser operators noticed two technical drawbacks of the double-frequency Nd:YAG laser: a long latency before retinal whitening (longest at the first spot and decreasing afterwards) and difficulty in performing some treatments on the peripheral retina because of problems in coupling the slit lamp with the laser beam.

## DISCUSSION

Francis L'Esperance was the first to attempt to replace gas ion lasers with a solid state laser in 1971 [5]. This laser used a flash lamp as pump source and a Nd:YAG rod combined with a frequency doubling crystal, instead of the ionic gas tube, as cavity. The resulting laser was far less cumbersome and emitted at 1,064 nm and 532 nm. Studies using infrared radiation (1,064 nm) indicated that photocoagulation of the retina frequently involved undesired effects, such as choroidal hemorrhages and rupture of Bruch's membrane [7]. These are probably caused by the use of high energy, necessary because of the low levels of infrared radiation absorbed by melanin. In our experience, these high energy levels also expose the patient to the risk of damage to the lens. These are the main reasons why 1,064 nm radiation is rarely used for retinal photocoagulation. However by filtering the infrared radiation and using only the visible component (532 nm), it is possible to produce radiation whose effects on tissue are very similar to monochromatic argon-green (514 nm) [8,9].

The first prototypes of double-frequency Nd:YAG, which emitted a monochromatic green radiation only, were produced in the late 1980s. The limitations of these systems were a tendency to overheat and low electrical-optical efficiency. Subsequently semiconductor diode lasers, emitting in the near infrared, were introduced into clinical practice as a possible replacement for gas ion lasers. These lasers are as effective as gas ion lasers, but the infrared radiation, which penetrates deep into the chorioretinal layers, makes it difficult to set the right energy level to achieve

correct retinal photocoagulation, avoiding chorioretinal scar enlargement and, sometimes, pain and choroidal effusion [10–15].

In the last few years technical improvements in frequency doubling crystal technology have led to the development of frequency-doubled Nd:YAG lasers of clinical utilility, which combine the advantages of solid state lasers with the emission of a monochromatic green wavelength. The arc lamp pumped, frequency-doubled Nd:YAG lasers offers the same technical advantages as solid-state lasers have over gas ion ones, which can be summarized as follows: long operating life-time, low maintenance costs, great reliability, compact size, air cooling system, standard voltage requirement, and low price. Furthermore all the histological data in the literature show a similarity between the chorioretinal lesions produced by the argon-green and the double-frequency Nd:YAG lasers [6,8,9,16–18].

The results of this study confirm the preliminary findings: the long-term efficacy of double-frequency Nd:YAG laser PRP in the treatment of PDR is similar to that of argon-green PRP. However we did encounter some drawbacks of the newer laser, mainly problems in coupling the slit lamp with laser emission, which sometimes make difficult to treat the peripheral retina, and a long latency before retinal whitening is seen (longer at the first spot but tending anyway to decrease later on). In some cases this latency makes difficult to treat the posterior pole. Although the long-term efficacy of PRP with the double-frequency Nd:YAG laser is similar to the Argon green laser, some improvements are still necessary to overcome these technical hurdles so as to replace ion-gas laser systems in clinical practice.

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